

# **In vitro recapitulation of biomimetic membranes: application to synaptic transmission**

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We have recently developed a novel microfluidic setup in which stable biomimetic membranes can be fabricated [1]. Fast and sensitive electric (patch-clamp) and optical (Confocal microscopy and single particle tracking) measurements allow the monitoring of the membrane state in time. During my presentation, I will describe how this new biomimetic membrane is made and demonstrate its versatility in terms of composition and usage. Then I'll show how this membrane can be used to monitor the nascent pore opening during the fusion of model synaptic vesicles and neuronal plasma membrane. First, I'll provide some hints on how sub-millisecond neurotransmission can be achieved accurately in time and space [2,3]. Then, I'll show the existence of small transient pores and correlate their discrete size with the number of molecular engines acting on their rim [4]. Finally, I'll discuss the topological nature of these transient pores.

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- [2] F. Manca, F. Pincet, L. Truskinovsky, J.E. Rothman, L. Foret, M. Caruel, *PNAS*, 116: 2435-2442 (2019).
- [3] S. Ramakrishnan, M. Bera, J. Coleman, S.S. Krishnakumar, F. Pincet, J.E. Rothman, *FEBS Letters*, 593 : 154- 162 (2019).
- [4] P. Heo, J. Coleman, J.-B. Fleury, J.E. Rothman, and F. Pincet, *PNAS*, 118: e202492211 (2021)